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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/022,014	12/14/2001	Charles K. Brush	10907-4	2793

22840 7590 05/11/2005

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,014	BRUSH ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *15-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This application has been transferred from Examiner Jeffrey Siew to Examiner Cynthia Wilder of Art Unit 1637. All future correspondence should be addressed to Examiner Cynthia Wilder whose contact information appears at the end of this Office Action.

Applicant filed an appeal brief on March 11, 2005. Upon further review of the prior art, finality of the rejections of the last Office action mailed on 11/24/2004 is withdrawn in view of new ground(s) of rejections. It is believed that this application is not ripe for appeal, as all of the issues have not bee fully developed on the record. The New grounds of rejections are set forth below. Claims 1-14 are pending. Claims 15-39 are withdrawn from consideration as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 102(b)

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Note* The claims are sufficiently broad to encompass multiple meaning. The specification does not provide a limiting definition of the terms recited therein. Accordingly, the preceding rejections are based on the Examiner's broad interpretation of the claims.

Claims 1, 10-13 rejected under 35 U.S.C. 102(b) as being anticipated by Monforte et al (US 5,830,655, November 3, 1998). Regarding claim 1, teach an assay comprising

contacting a target nucleic acid with a oligonucleotide immobilized on an array, under conditions that allow hybridization, said target nucleic acid having at least one phosphorothioate moiety (col. 6, lines 4-23 and col. 10, lines 1-63).

Regarding claim 10 and 12, Monforte et al teach the method of claim 1, wherein at least one nucleotide is a ribonucleotide or is a deoxynucleotide (col. 6, lines 18 and col. 10, line 1-2).

Regarding claims 11 and 13, Monforte et al teach the method of claims 10 or 12, wherein the target nucleic acid comprises from up to four different thiodeoxyribonucleotides. The reference also teaches the use thio- modified nucleosides (page col. 21, line 62 to col. 22, line 2). The reference further inherently implies the use of thio-ribonucleotides in the teaching of the target comprising RNA (page 10, lines 1-2, 10-14, 23-26 and 51-55). Therefore, Monforte et al meets the limitations of claims 1, 10-13 of the instant invention.

4. Claims 1-7, 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Wong et al (US 6,120,997, September 19, 2000). Regarding claim 1-3, Wong et al teach a method comprising contacting a target nucleic acid with probe immobilized on a microarray under conditions that allow hybridization, said target nucleic acid having at least one phosphorothioate moiety. Wong et al teach further comprising labeling said target nucleic acid by conjugating a reporter molecule to said phosphorothioate moiety (col. 8, lines 52-67, col. 28-32; col. 19, 42-48, and col. 20, lines 2-5).

Regarding claim 5-7, Wong et al teach the method of claim 2, wherein said reporter molecule has an electrophilic moiety comprising iodoacetamide (col. 19, lines 46-48).

Regarding claim 10, Wong et al teach wherein at least one nucleotide is a ribonucleotide (col. 19, lines 42-48). Therefore, Wong et al meets the limitations of claims 1-7 and 10 of the instant invention.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-8, 12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chee et al (WO 98/56954, December 1998) in view of Fidanza et al (Journal of American Chemical Society, Vol. 111, pages 9117-9119) and Housby et al (TIBTECH, vol. 18, pages 439-440, November 2000). Regarding claims 1-8, 12 and 14, Chee et al teach an expression assay, comprising contacting a target nucleic acid with a probe immobilized on an array under conditions that allow hybridization with said target and said probe, said target comprising a label, wherein said label is a florescent label or biotin. Chee et al further teach wherein at least one nucleotide is a ribonucleotide or deoxyribonucleotide and wherein said target is selected from the group consisting of RNA, DNA, cDNA or cRNA (page 4, line 10 to page 5, line 51; page 12, line 13-15, 23-25 and 31; page 15, lines 13-21).

Chee et al differs from the instant invention in that the reference does not teach wherein said target comprises a nucleic acid having at least one phosphorothioate moiety.

Fidanza et al teach the covalent attachment of reporter groups at specific sites within oligonucleotide sequences using phosphorothioate conjugation with iodacetamide.

Fidanza et al teaches that phosphorothioate diesters at specific sites within DNA fragments can be employed to direct the covalent attachment of reporter groups such as fluorophores spin labels, or drug derivatives to the sugar phosphate backbone. Fidanza et al further teaches that attaching reporter groups (covalently) wherein desired on the DNA backbone allow detailed studies in structure and function and should simplify studies involving protein binding (see entire reference, pages 9117-9119).

Housby et al provides a general teaching of microarrays and their use in methodologies, which relies on oligonucleotides conjugated with a phosphorothioate moiety. Housby et al teach that an obvious use for microarray technology is in the field of pharmacogenomics. Housby teach that Klaus Giese reported the identification of novel drug target using the proprietary GENEBLOC antisense technology and DNA arrays. Housby et al teach that the inhibitors are oligonucleotides that contain a mixture of 2' methyl ribose and deoxynucleotides with phosphorothioate modification of the phosphate backbone. Housby et al teach that Giese claimed that these molecules are specific for the intended target genes, have low toxicity, are resistant to nuclease and have a high target-binding affinity. Housby et al teach that it was suggested that these molecules might be useful in monitoring gene expression changes during disease progression, and also in studying the effects of gene inhibition on signaling pathways and differential gene expression (page 439, col. 2 and 3, entire section entitle "Pharmacogenomics").

One of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the detection method of Chee et al to encompass Fidanza et al's conjugation in order to increase facility of attaching reporter groups for the

benefit of studying structure and function of target nucleic acids as suggested by Fidanza et al.

One of ordinary skill in the art would have been further motivated to modify the detection method of Chee et al to encompass Fidanza et al's conjugation with a reasonable expectation of success based on the teaching of Housby et al that these molecules are specific for the intended target genes, have a high target-binding affinity and might be useful in monitoring gene expression during disease progression, gene inhibition of pathways and differential gene expression (see citation above).

7. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chee et al in view of Fidanza et al and Housby et al as applied to claims 1-8, 12 and 14 above, and further in view Karger et al (US 5,348,633,September 20, 1994). Regarding claim 9, Chee et al in view of Fidanza et al and Housby et al teach an expression assay and an array with probes which binds to labeled target nucleic acids, wherein said labeling comprises conjugating a reporter molecule (e.g., fluorophore) to a phosphorothioate moiety attached to the target.

The references differ from the instant invention in that they do not teach wherein said reporter molecule is TMR-maleimide, TMR-iodoacetamide or ALEXAFLUOR-maleimide.

Karger et al discloses et al use of reporter molecules in methods of labeling target molecules. Karger et al teach that a useful reporter molecule should possess strong absorbance and high fluorescence yield in order to produce a measurable signal during analysis. Karger et al further teach that the fluorophore should not photobleach

significantly during the method of detection and should be pH insensitive. Karger et al teach that the preferred reporter molecules as fluorescent labeling groups are tetramethylrhodamine iodoacetamide (col. 4, line 66 to col. 5, line 15).

One of ordinary skill in the art would have been motivated to have modified the detection method of Chee et al in view of Fidanza et al and Housby to encompass the use of the reporter molecule, tetramethylrhodamine iodoacetamide as the labeling group based on the characteristics and advantages taught by Karger et al that a molecule, such tetramethylrhodamine iodoacetamide possess strong absorbance, high fluorescence yield and produce a measurable signal during analysis.

Conclusion

8. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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